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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK, NY 10018

EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,347	BURCH ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 47-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 47-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/2/06 has been entered. Claims 38, 39 and 46-52 were pending. Applicants amended claim 38. In addition, Applicants canceled claims 39 and 46. Therefore, claims 38 and 47-52 are currently pending and examined on the merits.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

IDS

2. The Examiner respectfully requests resubmission of 1/25/02 IDS PTO-1449 form as this document cannot be found in the record.

Withdrawn Objections/Rejections

3. All pending rejections are hereby withdrawn in favor of the newly cited rejections below.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 38, 47, 48, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al. (U.S. Patent No. 4,569,937) (Date of Patent is **Feb 11, 1986**) in view of Furst (Furst, D. E. "Meloxicam: Selective COX-2 inhibition in clinical practice" *Seminars in Arthritis and Rheumatism*, **June 1997**, *26(1)*, 21-27).

For ***claim 38***, Baker et al. (see entire document) teach a method of effectively treating pain in humans comprising orally administering to a human patient an oral dosage form comprising two analgesic compounds and or pharmaceutically acceptable salts thereof (e.g., see abstract, "Pharmaceutical compositions of narcotic analgesics [i.e.,

compound #1] and ibuprofen [i.e., compound #2] have been found to exhibit unexpectedly enhanced analgesic activity [i.e., pain relief] ... This synergism enables the use of lower doses of either or both drugs [i.e., two analgesic compounds] with a concomitant reduction in risk of possible side effects"; see also column 3, paragraph 1 wherein administration to a "human" is disclosed; see also column 2, lines 44-48 wherein an "oral" dosage is disclosed, "Oxycodone ... are preferred because of their strong potency in oral dosage forms. Oxycodone is most preferred"; see also Examples, especially Example 1 wherein use pharmaceutical dosage forms containing "only" oxycodone and ibuprofen are set forth; see also columns 3-8 wherein "single dosage form" is disclosed; see also columns 8 and 9 wherein sequential administration is disclosed; see also columns 3 and 4 showing "sustained release" formulations). In addition, Baker et al. disclose the use of oxycodone and or at least one pharmaceutically acceptable salt in the composition (e.g., see column 2, lines 44-48 wherein an "oral" dosage is disclosed, "Oxycodone ... are preferred because of their strong potency in oral dosage forms. Oxycodone is most preferred"; see also columns 1, 2, 8-10; see also Examples, especially Example 1 wherein use pharmaceutical dosage forms containing "only" oxycodone and ibuprofen are set forth).

For ***claim 47***, Baker et al. disclose a ratio of oxycodone and/or at least one pharmaceutically acceptable salt thereof to NSAID and/or at least one pharmaceutically acceptable salt thereof is from about 0 0001:1 to about 1:1 (e.g., see column 2, lines 14-19, "(a) a narcotic analgesic [i.e., oxycodone], or a pharmaceutically acceptable salt thereof, and (b) ibuprofen [i.e., substituted by Meloxicam, see below], or a

pharmaceutically suitable salt thereof, in which the weight ratio of (a):(b) is from about 1:1 to about 1:800. Preferred ratios of (a):(b) are from about 1:3 to about 1:400, and most preferred ratios are from about 1:30 to about 1:400"; see also claim 1).

For ***claim 48***, Baker et al. teach oxycodone is present in the pharmaceutically acceptable salt form (e.g., see claim 1, "A pharmaceutical composition comprising a synergistic analgesic combination of (a) oxycodone, or pharmaceutically acceptable salt thereof").

For ***claim 51***, Baker et al. disclose the use of NSAID from about 0 5 mg to about 1500 mg (e.g., see Example 1 wherein 60 mg of Ibuprofen NSAID is disclosed; see also Examples 2-24; see also columns 2 and 3).

For ***claim 52***, Baker et al. disclose oxycodone in an amount from 2.5 mg to 800 mg (e.g., see Example 1 wherein 5 mg is disclosed; see also rest of Examples 2-24; see also column 2; see also column 3, dosage forms section).

The prior art teachings of Baker et al. differ from the claimed invention as follows:

For ***claim 38, 47, 48, 51 and 52***, Baker et al. fail to disclose compositions with Meloxicam. Baker et al. only teach the use of NSAIDs like ibuprofen (e.g., see Baker et al., abstract)

However, Furst teach the following limitations that are deficient in Baker et al.:

For ***claim 38, 47, 48, 51 and 52***, Furst (see entire document) teach the use of Meloxicam to alleviate pain in human patients (e.g., see figure 1; see also page 23, column 2, paragraph 1 "Nabumetone was significantly ... more effective than placebo

and had comparable efficacy to naproxen or aspirin in the physicians' and patients' assessment of degree of pain ... [further studies] showed meloxicam [7.5 mg] to have efficacy approximately equal to that of nabumetone 1,000 mg"). Thus, Meloxicam is even more effective than other NSAIDs like Nabumetone at reducing pain and can be used in smaller dosages (i.e., 7.5 mg compare to 1,000 mg). Furthermore, Meloxicam exhibits less serious gastric and renal side effects than ibuprofen because it selectively inhibits COX-2 rather than COX-1 (e.g., see abstract, "inhibition of the COX-1 isoform produces the troublesome and sometimes serious gastric and renal side effects of NSAIDs. A relatively selective COX-2 inhibitor, such as meloxicam, may ... [exhibit] improved tolerability"; see also page 22, column 1, last paragraph, "Meloxicam exhibited greater COX-2 selectivity than ... ibuprofen ... [which] preferentially inhibited COX-1"; see also "Safety of Meloxicam" section starting on page 24, especially, column 2, paragraph 1, "Meloxicam 7.5 mg caused no significant change in the mucosal appearance ... With piroxicam, there was a significantly higher number of endoscopically detected ulcers developing during the study compared with the meloxicam 15 mg group"; see also figure 2; see also page 24, column 2, paragraph 2, "During this large 4-week trial, GI side effects were significantly more common in the diclofenac group (19%) than in the meloxicam group (13%) ... diclofenac caused significantly more dyspepsia, abdominal pain, nausea and vomiting, and diarrhea than meloxicam"; see also Table 2 showing meloxicam to be the "safest" NSAID especially with regard to gastrointestinal events; see also page 26, column 1, paragraph 1 showing meloxicam to be "well suited for the elderly" because the drug is "almost entirely converted to inactive metabolites before

excretion"; see also Figure 3; see also Conclusions section, especially page 26, column 2, last paragraph, "Taken together, these results show that meloxicam has a good safety and efficacy profile, with some indication of increased GI safety over several other NSAIDs. The possible explanation for this profiles meloxicam's relatively selective inhibition of COX-2").

For ***claim 51***, Furst also disclose, for example, 7.5 and 15 mg doses (e.g., see Table 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substituted Meloxicam as taught by Furst for the ibuprofen in the ibuprofen/oxycodone compositions as taught by Baker et al. because Furst et al. shows that meloxicam is more potent than any other NSAID at reducing pain in clinical trials (e.g., see figure 2). Furthermore, a person of skill in the art would have been motivated to use Meloxicam not only because it is more potent but also because it is safer than other NSAIDs including the ibuprofen disclosed by Baker et al. (e.g., see see abstract, "inhibition of the COX-1 isoform produces the troublesome and sometimes serious gastric and renal side effects of NSAIDs. A relatively selective COX-2 inhibitor, such as meloxicam, may ... [exhibit] improved tolerability"; see also page 22, column 1, last paragraph, "Meloxicam exhibited greater COX-2 selectivity than ... ibuprofen ... [which] preferentially inhibited COX-1"; see also "Safety of Meloxicam" section starting on page 24, especially, column 2, paragraph 1, "Meloxicam 7.5 mg caused no significant change in the mucosal appearance ... With piroxicam, there was a significantly higher number of endoscopically detected ulcers developing during the study compared with the

meloxicam 15 mg group"; see also figure 2; see also page 24, column 2, paragraph 2, "During this large 4-week trial, GI side effects were significantly more common in the diclofenac group (19%) than in the meloxicam group (13%) ... diclofenac caused significantly more dyspepsia, abdominal pain, nausea and vomiting, and diarrhea than meloxicam"; see also Table 2 showing meloxicam to be the "safest" NSAID especially with regard to gastrointestinal events; see also page 26, column 1, paragraph 1 showing meloxicam to be "well suited for the elderly" because the drug is "almost entirely converted to inactive metabolites before excretion"; see also Figure 3; see also Conclusions section, especially page 26, column 2, last paragraph, "Taken together, these results show that meloxicam has a good safety and efficacy profile, with some indication of increased GI safety over several other NSAIDs. The possible explanation for this profiles meloxicam's relatively selective inhibition of COX-2"). Finally, a person of skill in the art would reasonably have expected to be successful because Meloxicam has been shown through extensive human clinical trials to be safe and effective especially with regard to the gastrointestinal tract (see Furst citations above), which is a preferred route of administration disclosed by Baker et al. (e.g., see Baker et al., column 4, line 13). In addition, Baker et al. explicitly state in the Background section that NSAIDs have been used to treat pain (e.g., see Baker et al., column 1, paragraph 3, "This patent discloses that the analgesic effect of the combination of a selected NSAID and a selected narcotic analgesic is greater than for either alone which analgesic effect"), which would include Meloxicam (e.g., see abstract, "Nonsteroidal antiinflammatory drugs (NSAIDs) exert their actions by inhibiting cyclooxygenase (COX) ... A relatively selective COX-2

inhibitor ... [is] meloxicam [i.e., Meloxicam is an NSAID]"). Furthermore, Furst explicitly state that it is safer than ibuprofen (e.g., see Furst, page 22, column 1, last paragraph) that was disclosed by Baker et al. (e.g., see abstract).

6. Claims 38 and 47-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al. (U.S. Patent No. 4,569,937) (Date of Patent is Feb 11, 1986) in view of Furst (Furst, D. E. "Meloxicam: Selective COX-2 inhibition in clinical practice" Seminars in Arthritis and Rheumatism, June 1997, 26(1), 21-27) and in further view of Oshlack I et al. US Pat. No. 5,472,712 (12/95) and/or Oshlack II et al. US Pat. No. 6,294,195 (9/01: effectively filed 10/93 or earlier) and Iyengar et al. (WO 97/25988) (Date of Patent is **July 24, 1997**).

For ***claims 38, 47, 48, 51 and 52***, Furst and Baker et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 38, 47, 48, 51 and 52.

The combined prior art references of Furst and Baker et al. differ from the claimed invention as follows:

For ***claim 49***, the combined references of Furst and Baker et al. fail to teach the use of "a sustained release carrier which provides a sustained release of the oxycodone and/or ... salt thereof."

For ***claim 50***, the combined references of Furst and Baker et al. fail to teach the use of a sustained release of the meloxicam and/or salt thereof.

However, the combined references of Oshlack I/II et al. and Iyengar et al. teach the following limitations that are deficient in Furst and Baker et al.:

For ***claim 49***, the combined references of Oshlack I/II et al. and Iyengar et al. (see entire documents) teach the use of sustained release dosage forms for opioid analgesics, including oxycodone, which utilize sustained release carriers employing beads which are coated with the opioid drug or which include substrate layers which include the drugs is known in the art to effectuate delayed release of extended duration (e.g., see Oshlack I, abstract, "A stabilized solid controlled release formulation ..."; see also column 14, paragraph 2, "A wide variety of therapeutically active agents can be used in conjunction with the present invention ... [including] oxycodone"; see also column 13, line 34; see also claim 6; see also claim 50; see also claim 62; see also claim 86; see also claim 108; see also Oshlack II, abstract, see also claims; see also examples; see also column 6, line 48; see also claim 5).

For ***claim 50***, the combined references of Oshlack I/II et al. and Iyengar et al. also teach the use of sustained release for Meloxicam (e.g., see Iyengar et al., paragraph bridging pages 46 and 47, "The present invention encompasses ... Meloxicam"; see also page 47, first full paragraph, "The advantages of any synergistic combination therapy are obvious ... Sustained release formulations are now more feasible due to the lower amounts of active ingredient necessary"; see also paragraph bridging pages 48 and 49, "The compositions of the invention can be formulated so as to provide quick, sustained or delayed release of the active ingredient after administration to the patient by employing procedures known in the art").

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize sustained release carriers for oxycodone including beads/layers as taught by the the combined references of Oshlack I/II et al. and Iyengar for use in the Baker compositions since Baker specifically teaches using "sustained release formulations." Furthermore, a person of ordinary skill in the art would have been motivated to use these formulations to delay drug release for extended duration (e.g., see Oshclack II, abstract, ""provide effective blood levels of the opioid analgesic for at least about 24 hours"). In addition, a person of skill in the art would have been motivated to use oxycodone in a sustained release dosage because, according to Oschlack I, "The present invention provides many benefits over prior art coatings, including, but not limited to, avoidance of organic solvents which have inherent safety concerns (flammability, carcinogenicity, environmental concerns, safety in general), and extended stability which may result in extended shelf life and expiration dating" (e.g., see Oschlack I, column 5, paragraph 3). Furthermore, Oshclack II state, "provide effective blood levels of the opioid analgesic for at least about 24 hours" using controlled release (e.g., see abstract). Finally, a person of skill in the art would have reasonably expected to be successful because the combined references of Oshlack I/II et al. and Iyengar teach that these formulations can be used for opioid analgesics like Applicants' preferred oxycodone or NSAIDs like Applicants' preferred Meloxicam (e.g., see Oshlack I, claims 6, 50, 62, 86 and 108; see also Iyengar et al., paragraph bridging pages 46 and 47, "The present invention encompasses ... Meloxicam"; see also page 47, first full paragraph, "The advantages of any synergistic combination therapy are obvious ... Sustained release

formulations are now more feasible due to the lower amounts of active ingredient necessary"; see also paragraph bridging pages 48 and 49, "The compositions of the invention can be formulated so as to provide quick, sustained or delayed release of the active ingredient after administration to the patient by employing procedures known in the art").

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
November 27, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER